

Amendments to the Claims

Please amend Claims 1-7, 15 and 18-19.

Please add new Claims 20-33.

Please cancel Claims 8-14 and 17.

The claim listing will replace all prior versions of the claims in the application.

Claim Listing

1. (Currently Amended) A method of ~~treating~~ inhibiting TNF α in a human patient having a neurodegenerative ~~inflammation in a human in need thereof disease~~, comprising administering to the cerebrospinal fluid (CSF) of said human patient an effective TNF-~~inhibiting~~ TNF α -inhibiting amount of an anti-TNF anti-TNF α antibody or TNF-binding antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation~~, said anti-TNF α antibody comprising a human constant region, wherein said anti-TNF α antibody or antigen-binding fragment thereof (i) competitively inhibits binding of A2 (ATCC Accession No. PTA-7045) to human TNF α and (ii) binds to a neutralizing epitope of human TNF α with an affinity of at least 1×10^8 liter/mole, measured as an association constant (K_a), as determined by Scatchard analysis.
2. (Currently Amended) A method of ~~treating~~ inhibiting TNF α in a human patient having a neurodegenerative ~~inflammation in a human in need thereof disease~~, comprising administering to the cerebrospinal fluid (CSF) of said human patient an effective TNF-~~inhibiting~~ TNF α -inhibiting amount of an anti-TNF anti-TNF α monoclonal antibody or TNF-binding antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation, wherein said anti-TNF antibody or fragment is a chimeric TNF antibody~~, said anti-TNF α antibody comprising a human constant region, wherein said anti-TNF α chimeric antibody or antigen-binding fragment thereof (i) comprises the antigen-binding regions of A2 (ATCC Accession No. PTA-7045) and (ii) binds to a neutralizing epitope of human TNF α with an affinity of at least 1×10^8 liter/mole, measured as an association constant (K_a), as determined by Scatchard analysis.

3. (Currently Amended) A method of ~~treating~~ inhibiting TNF α in a human patient having a neurodegenerative inflammation in a human in need thereof disease, comprising administering to ~~the cerebrospinal fluid (CSF) of said human patient~~ an effective TNF-~~inhibiting~~ TNF α -inhibiting amount of an ~~anti-TNF~~ anti-TNF α antibody or ~~TNF-binding~~ antigen-binding fragment thereof ~~sufficient to treat the neurodegenerative inflammation~~, said anti-TNF α antibody comprising a human IgG1 constant region, wherein said ~~anti-TNF~~ anti-TNF α antibody or antigen-binding fragment thereof (i) competitively inhibits the binding of TNF to the ~~TNF antibody cA2-A2 (ATCC Accession No. PTA-7045)~~ to human TNF α and (ii) binds to a neutralizing epitope of human TNF α *in vivo* with an affinity of at least 1×10^8 liter/mole, measured as an association constant (K_a), as determined by Scatchard analysis.
4. (Currently Amended) The method of Claim 3, wherein the ~~chimeric TNF~~ anti-TNF α antibody comprises a non-human variable region.
5. (Currently Amended) The method of Claim 1, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNF α antibody or fragment thereof.
6. (Currently Amended) The method of Claim 2, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNF α antibody or fragment thereof.
7. (Currently Amended) The method of Claim 3, wherein said administration comprises a single or divided ~~0.1 - 100 mg/kg~~ 0.1 - 50 mg/kg dose of said ~~anti-TNF~~ anti-TNF α antibody or fragment thereof.

Claims 8.-14. (Canceled).

15. (Currently Amended) The method of ~~Claim 8, wherein the therapeutic agent is Claim 1~~ further comprising administering to the human an effective amount of a pain control agent.
16. (Original) The method of Claim 15, wherein the pain control agent is selected from the group consisting of: paracetamol and dextropropoxyphene.

Claim 17. (Canceled).

18. (Currently Amended) The method of Claim 1, wherein the ~~anti-TNF chimeric~~ anti-TNF α antibody is of immunoglobulin class IgG1, IgG2, IgG3, IgG4 or IgM.
19. (Currently Amended) The method of Claim 1, wherein the ~~anti-TNF chimeric~~ anti-TNF α antibody is a fragment selected from the group consisting of Fab, Fab', F(ab')₂ and Fv.
20. (New) The method of Claim 5 wherein said single or divided dose is one selected from 0.5, 0.9, 1, 1.1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 mg/kg per day on at least one of day 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or at least one of week 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20.
21. (New) The method of Claim 1, wherein said Scatchard analysis comprises labeling the anti-TNF α antibody or antigen-binding fragment thereof and measuring direct binding of ¹²⁵I labeled anti-TNF α antibody or antigen-binding fragment thereof to immobilized rhTNF α , and wherein said antibodies are labelled to a specific activity of about 9.7 μ Ci/ μ g by the iodogen method.
22. (New) The method of Claim 1, wherein the anti-TNF α antibody or antigen-binding fragment comprises a human constant region and a human variable region.

23. (New) The method of Claim 1 wherein said anti-TNF α antibody or antigen-binding fragment comprises at least one human light chain and at least one human heavy chain.
24. (New) The method of Claim 1, wherein said anti-TNF α antibody or antigen-binding fragment is administered to the human by means of parenteral administration.
25. (New) The method of Claim 1, wherein said anti-TNF α antibody or antigen-binding fragment is administered to the human by means of intravenous administration, subcutaneous administration or intramuscular administration.
26. (New) The method of Claim 23, wherein the light chain comprises all antigen-binding regions of the light chain of A2 (ATCC Accession No. PTA-7045).
27. (New) The method of Claim 23, wherein the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045).
28. (New) The method of Claim 23, wherein the light chain comprises all antigen-binding regions of the light chain of A2 (ATCC Accession No. PTA-7045) and the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045).
29. (New) The method of Claim 1, further comprising administering a composition comprising the anti-TNF α antibody or antigen-binding fragment of Claim 1 and a pharmaceutically acceptable carrier.
30. (New) The method of Claim 1, wherein said anti-TNF α antibody or antigen-binding fragment has specificity for a neutralizing epitope of human TNF α .

31. (New) The method of Claim 1, wherein said anti-TNF α antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:5.
32. (New) The method of Claim 31, wherein the non-human variable region is murine.
33. (New) The method of Claim 32, wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.